STXBP1 encephalopathy with epilepsy

STXBP1 encephalopathy with epilepsy is a condition characterized by recurrent seizures (epilepsy), abnormal brain function (encephalopathy), and intellectual disability. The signs and symptoms of this condition typically begin in infancy but can first appear later in childhood or early adulthood. In many affected individuals, seizures stop in early childhood with the other neurological problems continuing throughout life. However, some people with *STXBP1* encephalopathy with epilepsy have seizures that persist.

The most common seizures in *STXBP1* encephalopathy with epilepsy are infantile spasms, which occur before age 1 and consist of involuntary muscle contractions. Other seizure types that can occur in infants with this condition include involuntary muscle twitches (myoclonic seizures), sudden episodes of weak muscle tone (atonic seizures), partial or complete loss of consciousness (absence seizures), or loss of consciousness with muscle rigidity and convulsions (tonic-clonic seizures). Most people with *STXBP1* encephalopathy with epilepsy have more than one type of seizure. In about one-quarter of individuals, the seizures are described as refractory because they do not respond to therapy with anti-epileptic medications.

Other signs and symptoms of *STXBP1* encephalopathy with epilepsy include intellectual disability that is often moderate to profound. Affected individuals also have delayed development of speech and walking; in some, these skills never fully develop. Movement and behavior disorders may also occur. Many affected individuals have feeding difficulties. In some cases, areas of brain tissue loss (atrophy) have been found on medical imaging.

Frequency

The prevalence of *STXBP1* encephalopathy with epilepsy is unknown. At least 200 individuals with this condition have been described in the medical literature.

Causes

As its name indicates, *STXBP1* encephalopathy with epilepsy is caused by mutations in the *STXBP1* gene. This gene provides instructions for making syntaxin-binding protein 1. In nerve cells (neurons), this protein helps regulate the release of chemical messengers called neurotransmitters from compartments known as synaptic vesicles. The release of neurotransmitters relays signals between neurons and is critical for normal brain function.

STXBP1 gene mutations reduce the amount of functional protein produced from the gene, which impairs the release of neurotransmitters from neurons. A change in neurotransmitter levels can lead to uncontrolled activation (excitation) of neurons,

which causes seizures. This altered neuronal activity does not appear to impair the development or survival of neurons; the cause of the encephalopathy and other neurological problems in this condition is unclear.

Inheritance Pattern

This condition is inherited in an autosomal dominant pattern, which means one copy of the altered gene in each cell is sufficient to cause the disorder.

Most cases of this condition result from new (de novo) mutations in the gene that occur during the formation of reproductive cells (eggs or sperm) in an affected individual's parent or in early embryonic development. These cases occur in people with no history of the disorder in their family.

Other Names for This Condition

- early-infantile epileptic encephalopathy 4
- EIEE4
- STXBP1 epileptic encephalopathy
- STXBP1-related early-onset encephalopathy
- STXBP1-related epileptic encephalopathy

Diagnosis & Management

Genetic Testing Information

- What is genetic testing?
  /primer/testing/genetictesting
- Genetic Testing Registry: Early infantile epileptic encephalopathy 4
  https://www.ncbi.nlm.nih.gov/gtr/conditions/C2677326/

Research Studies from ClinicalTrials.gov

- ClinicalTrials.gov
  https://clinicaltrials.gov/ct2/results?cond=%22STXBP1+encephalopathy+with+epilepsy%22+OR+%22STXBP1+epileptic+encephalopathy%22+OR+%22early-infantile+epileptic+encephalopathy+4%22+OR+%22early-onset+epileptic+encephalopathy%22

Other Diagnosis and Management Resources

- GeneReview: STXBP1 Encephalopathy with Epilepsy
  https://www.ncbi.nlm.nih.gov/books/NBK396561

Additional Information & Resources

Health Information from MedlinePlus

- Health Topic: Epilepsy
  https://medlineplus.gov/epilepsy.html

Genetic and Rare Diseases Information Center

- Early infantile epileptic encephalopathy 4
  https://rarediseases.info.nih.gov/diseases/12900/early-infantile-epileptic-encephalopathy-4

Additional NIH Resources

- National Institute of Neurological Disorders and Stroke: Encephalopathy Information Page
  https://www.ninds.nih.gov/Disorders/All-Disorders/Encephalopathy-Information-Page
- National Institute of Neurological Disorders and Stroke: Epilepsy Information Page
  https://www.ninds.nih.gov/Disorders/All-Disorders/Epilepsy-Information-Page

Educational Resources

- Boston Children's Hospital: Epilepsy and Seizure Disorder in Children
  https://www.childrenshospital.org/Conditions-and-Treatments/Conditions/E/Epilepsy
- Centers for Disease Control and Prevention: Epilepsy
  https://www.cdc.gov/epilepsy/index.html
- Centers for Disease Control and Prevention: Facts About Developmental Disabilities
  https://www.cdc.gov/ncbddd/developmentaldisabilities/facts.html
- MalaCards: epileptic encephalopathy, early infantile, 4
  https://www.malacards.org/card/epileptic_encephalopathy_early_infantile_4
- MalaCards: stxbp1 encephalopathy with epilepsy
  https://www.malacards.org/card/stxbp1_encephalopathy_with_epilepsy
- Merck Manual Consumer Version: Seizure Disorders
  https://www.merckmanuals.com/home/brain,-spinal-cord,-and-nerve-disorders/seizure-disorders/seizure-disorders
- Orphanet: Early infantile epileptic encephalopathy
  https://www.orpha.net/consor/cgi-bin/OC_Exp.php?Lng=EN&Expert=1934
- Unique: Rare Chromosome Disorder Support Group (UK)
  https://www.rarechromo.org/media/singlegeneinfo/Single%20Gene%20Disorder%20Guides/STXBP1%20Disorders%20QFN.pdf

Patient Support and Advocacy Resources

- American Association on Intellectual and Developmental Disabilities (AAIDD)
  https://www.aaidd.org/
- American Epilepsy Society
  https://www.aesnet.org/
- CURE: Citizens United for Research in Epilepsy
  https://www.cureepilepsy.org/
- Epilepsy Canada
  https://www.epilepsy.ca/
- Epilepsy Society (UK)
  https://www.epilepsysociety.org.uk/
- Medical Home Portal: Seizures/Epilepsy
  https://www.medicalhomeportal.org/diagnoses-and-conditions/seizures-epilepsy

Clinical Information from GeneReviews

- STXBP1 Encephalopathy with Epilepsy
  https://www.ncbi.nlm.nih.gov/books/NBK396561

Scientific Articles on PubMed

- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28%28STXBP1%5BTI%5D%29+AND+%28encephalopathy%5BTI%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+1800+days%22%5Bdp%5D

Catalog of Genes and Diseases from OMIM

- EPILEPTIC ENCEPHALOPATHY, EARLY INFANTILE, 4
  http://omim.org/entry/612164

Medical Genetics Database from MedGen

- Early infantile epileptic encephalopathy 4
  https://www.ncbi.nlm.nih.gov/medgen/436917

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